

1. GENERATE
ENSEMBLE

20,000 CONFORMATIONAL STATES

2. CALCULATE
GIBBS ENERGY

20,000 ΔG VALUES

3. IDENTIFY ΔG s OF
BINDING COMPETENT
STATES

"a" bc ΔG s "20,000-a" non-bc ΔG s

4. MODIFY bc ΔG s

"a" bc ΔG^* s

5. FORM TWO SETS
OF ΔG VALUES,
WITH AND W/O
LIGAND

20,000 ΔG s + ligand
bc ΔG^* s non-bc ΔG s

20,000 ΔG s - ligand
bc ΔG s non-bc ΔG s

6. COMPUTE
PROBABILITIES

20,000 P^* s + ligand
bc P^* s non-bc P s

20,000 P s - ligand
bc P s non-bc P s

7. CALCULATE
STABILITY
CONSTANTS

$n_{ik} + \text{ligand}$
 K_s

$n_{ik} - \text{ligand}$
 K_s

8. COMPARE K
VALUES AND
SELECT AFFECTED
RESIDUES

9. CREATE AND
DISPLAY MODEL

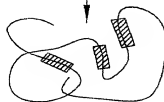


FIG. 1

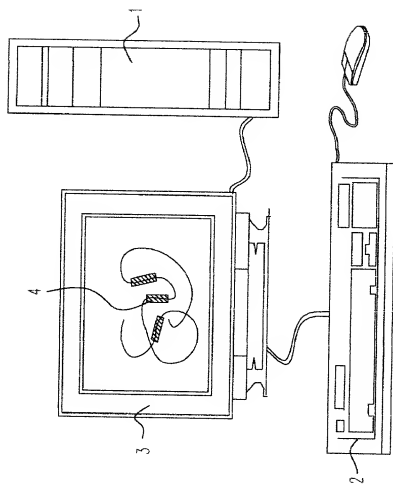


FIG. 2

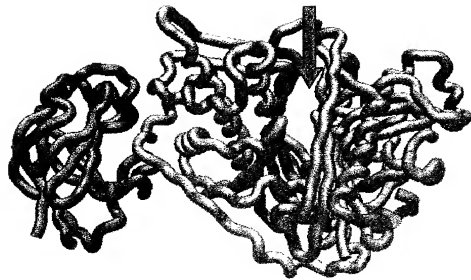


FIG. 3A

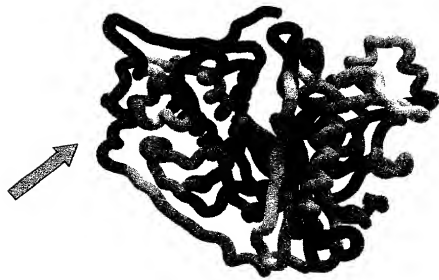


FIG. 3B

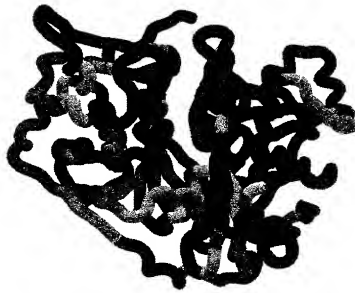


FIG. 3C